

APPLICANT: Stanley T. Crooke
SERIAL NO: 09/479,783

DOCKET NO: ISIS-4313

AMENDMENTS TO THE CLAIMS: This listing of claims replaces all prior versions and listings of claims in the instant patent application.

Listing of claims:

1-80. (Canceled).

81. (Currently amended) An affinity matrix comprising ~~the composition of claim 78~~ a composition which comprises a duplex of a first oligonucleotide and a second oligonucleotide, wherein:

each of said first and said second oligonucleotides is eight to fifty nucleoside subunits in length;

said first and said second oligonucleotides are not covalently linked;

each of said first and said second oligonucleotides have a central portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said central portions are base-paired with each other in said duplex; and

at least one of said first and said second oligonucleotides has portions flanking said central portions having chemical modifications which increase their resistance to single-stranded nucleases and increase their affinity for the other oligonucleotide of the duplex.

82-92. (Canceled).

93. (Currently amended) A composition of ~~claim 78, wherein comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein:~~

each of said first and said second oligonucleotides is eight to fifty nucleoside subunits in length;

said first and said second oligonucleotides are not covalently linked;

each of said first and said second oligonucleotides have a central portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said central portions are base-paired with each other in said duplex;

at least one of said first and said second oligonucleotides has portions flanking said central portions having chemical modifications which increase their resistance to single-stranded nucleases and increase their affinity for the other oligonucleotide of the duplex; and

one of said oligonucleotides has the nucleotide sequence of SEQ ID NO: 8.

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94-105. (Canceled).

106. (Currently amended) A composition comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein each of said first and said second oligonucleotides is eight to fifty nucleoside subunits in length, wherein said first and said second oligonucleotides have a central portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages, wherein said central portions are base-paired with each other in said duplex, wherein at least one of said first and said second oligonucleotides has portions flanking said central portions, said portions having chemical modifications which increase their resistance ~~make them resistant~~ to single-stranded nucleases, and wherein one of said oligonucleotides has the nucleotide sequence of SEQ ID NO: 8.

107-175. (Canceled)

176. (Previously presented) The composition of claim 106 wherein said chemical modifications are phosphorothioate linkages.

177. (Previously presented) The composition of claim 106 wherein said chemical modifications are 2'-methoxy modifications.

178. (Previously presented) The composition of claim 106 wherein said chemical modifications are 2'-fluoro modifications.

179. (Currently amended) The composition of claim 106 wherein said chemical modifications are ~~2'-O-methoxyethoxy~~ 2'-O-methoxyethyl modifications.

180. (Previously presented) The composition of claim 106 wherein one of said first and said second oligonucleotides is twelve to thirty nucleoside subunits in length.

181. (Previously presented) The composition of claim 106 wherein one of said first and said second oligonucleotides is fifteen to twenty-five nucleoside subunits in length.

182. (Previously presented) A composition comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein:

each of said first and said second oligonucleotides is about 17 to about 20 nucleoside subunits in length;

said first and said second oligonucleotides are not covalently linked;

each of said first and said second oligonucleotides comprise a portion with at least

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four consecutive ribofuranosyl residues, wherein said portions are base-paired with each other in said duplex; and

at least one of said first and said second oligonucleotides comprises chemical modifications that increase its resistance to single-stranded nucleases.

183. (Previously presented) The composition of claim 182 wherein said portions have phosphodiester linkages.

184. (Previously presented) The composition of claim 182 wherein the chemical modifications are 2'-methoxy modifications.

185. (Previously presented) The composition of claim 182 wherein the chemical modifications are 2'-fluoro modifications.

186. (Currently amended) The composition of claim 182 wherein the chemical modifications are ~~2'-O-methoxyethoxy~~ 2'-O-methoxyethyl modifications.

187. (Previously presented) The composition of claim 182 wherein the chemical modifications are phosphorothioate linkages.

188. (Previously presented) The composition of claim 182 wherein at least one oligonucleotide further comprises at least one chemical modification that increases its affinity for the other oligonucleotide.

189. (Currently amended) The composition of claim 182 wherein at least ~~[[of]]~~ one of said first and said second oligonucleotides is 17 ~~nucleobase~~ nucleoside subunits in length.

190. (Currently amended) The composition of claim 189 wherein each of said first and said second oligonucleotides is 17 ~~nucleobase~~ nucleoside subunits in length.

191. (Currently amended) The composition of claim 182 wherein at least of one of said first and said second oligonucleotides is 20 ~~nucleobase~~ nucleoside subunits in length.

192. (Currently amended) The composition of claim ~~[[189]]~~ 191 wherein each of said first and said second oligonucleotides is 20 ~~nucleobase~~ nucleoside subunits in length.

193. (Previously presented) The composition of claim 182 which activates a double-stranded RNA nuclease.

194. (New) A composition comprising a duplex of a first oligonucleotide and a

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second oligonucleotide, wherein:

each of said first and said second oligonucleotides is independently 15 to 25 nucleoside subunits in length;

said first and said second oligonucleotides are not covalently linked;

each of said first and said second oligonucleotides comprise a portion with at least four consecutive ribofuranosyl residues, wherein said portions are base-paired with each other in said duplex; and

at least one of said first and said second oligonucleotides comprises at least one chemical modification that increases its resistance to single-stranded nucleases or increases its affinity for the other oligonucleotide.

195. (New) The composition of claim 194 wherein at least one chemical modification is a modified internucleoside linkage, a modified sugar moiety or a modified nucleobase.

196. (New) The composition of claim 194 wherein at least one chemical modification is a phosphorothioate linkage.

197. (New) The composition of claim 194 wherein at least one chemical modification is a 2'-substituted sugar modification.

198. (New) The composition of claim 194 wherein at least one chemical modification is a 2'-alkoxy sugar modification.

199. (New) The composition of claim 194 wherein at least one chemical modification is a 2'-methoxy modification.

200. (New) The composition of claim 194 wherein at least one chemical modification is a 2'-fluoro modification.

201. (New) The composition of claim 194 wherein at least one chemical modification is a 2'-O-methoxyethyl modification.

202. (New) The composition of claim 194 wherein each of said first and said second oligonucleotides independently comprise at least one chemical modification that increases its resistance to single-stranded nucleases or increases its affinity for the other oligonucleotide.

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203. (New) The composition of claim 194 wherein said first and said second oligonucleotide comprise at least 17 contiguous nucleotides which are 100% complementary to each other.

204. (New) A composition comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein:

each of said first and said second oligonucleotides is independently 8 to 50 nucleoside subunits in length;

said first and said second oligonucleotides are not covalently linked;

each of said first and said second oligonucleotides comprise a portion with at least four consecutive ribofuranosyl residues, wherein said portions are base-paired with each other in said duplex; and

each of said first and said second oligonucleotides independently comprise at least one chemical modification that increases its resistance to single-stranded nucleases or increases its affinity for the other oligonucleotide.

205. (New) The composition of claim 204 wherein at least one chemical modification is a modified internucleoside linkage, a modified sugar moiety or a modified nucleobase.

206. (New) The composition of claim 204 wherein at least one chemical modification is a phosphorothioate linkage.

207. (New) The composition of claim 204 wherein at least one chemical modification is a 2'-substituted sugar modification.

208. (New) The composition of claim 204 wherein at least one chemical modification is a 2'-alkoxy sugar modification.

209. (New) The composition of claim 204 wherein at least one chemical modification is a 2'-methoxy modification.

210. (New) The composition of claim 204 wherein at least one chemical modification is a 2'-fluoro modification.

211. (New) The composition of claim 204 wherein at least one chemical modification is a 2'-O-methoxyethyl modification.

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212. (New) The composition of claim 204 wherein at least one of said first and said second oligonucleotides is 12 to 30 nucleoside subunits in length.

213. (New) The composition of claim 204 wherein at least one of said first and said second oligonucleotides is 15 to 25 nucleoside subunits in length.

214. (New) A composition comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein:

each of said first and said second oligonucleotides is independently 8 to 50 nucleoside subunits in length;

said first oligonucleotide is 100% complementary to said second oligonucleotide;

said first and said second oligonucleotides are not covalently linked;

each of said first and said second oligonucleotides comprise a portion with at least four consecutive ribofuranosyl residues, wherein said portions are base-paired with each other in said duplex; and

at least one of said first and said second oligonucleotides comprises at least one chemical modification that increases its resistance to single-stranded nucleases or increases its affinity for the other oligonucleotide.

215. (New) The composition of claim 214 wherein at least one chemical modification is a modified internucleoside linkage, a modified sugar moiety or a modified nucleobase.

216. (New) The composition of claim 214 wherein at least one chemical modification is a phosphorothioate linkage.

217. (New) The composition of claim 214 wherein at least one chemical modification is a 2'-substituted sugar modification.

218. (New) The composition of claim 214 wherein at least one chemical modification is a 2'-alkoxy sugar modification.

219. (New) The composition of claim 214 wherein at least one chemical modification is a 2'-methoxy modification.

220. (New) The composition of claim 214 wherein at least one chemical modification is a 2'-fluoro modification.

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221. (New) The composition of claim 214 wherein at least one chemical modification is a 2'-O-methoxyethyl modification.

222. (New) The composition of claim 214 wherein at least one of said first and said second oligonucleotides is 12 to 30 nucleoside subunits in length.

223. (New) The composition of claim 214 wherein at least one of said first and said second oligonucleotides is 15 to 25 nucleoside subunits in length.

224. (New) The composition of claim 214 wherein each of said first and said second oligonucleotides independently comprises at least one chemical modification that increases its resistance to single-stranded nucleases or increases its affinity for the other oligonucleotide.

225. (New) A composition comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein:

each of said first and said second oligonucleotides is about 17 to about 20 nucleoside subunits in length;

said first and said second oligonucleotides are not covalently linked;

each of said first and said second oligonucleotides comprise a portion with at least four consecutive ribofuranosyl residues, wherein said portions are base-paired with each other in said duplex; and

at least one of said first and said second oligonucleotides comprises at least one chemical modification that increases its resistance to single-stranded nucleases or increases its affinity for the other oligonucleotide.

226. (New) The composition of claim 225 wherein at least one chemical modification is a modified internucleoside linkage, a modified sugar moiety or a modified nucleobase.

227. (New) The composition of claim 225 wherein at least one chemical modification is a phosphorothioate linkage.

228. (New) The composition of claim 225 wherein at least one chemical modification is a 2'-substituted sugar modification.

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229. (New) The composition of claim 225 wherein at least one chemical modification is a 2'-alkoxy sugar modification.

230. (New) The composition of claim 225 wherein at least one chemical modification is a 2'-methoxy modification.

231. (New) The composition of claim 225 wherein at least one chemical modification is a 2'-fluoro modification.

232. (New) The composition of claim 225 wherein at least one chemical modification is a 2'-O-methoxyethyl modification.

233. (New) The composition of claim 225 wherein each of said first and said second oligonucleotides independently comprises at least one chemical modification that increases its resistance to single-stranded nucleases or increases its affinity for the other oligonucleotide.

234. (New) A composition comprising a duplex of a first oligonucleotide and a second oligonucleotide, wherein:

each of said first and said second oligonucleotides is independently 15 to 25 nucleoside subunits in length;

said first and said second oligonucleotides are not covalently linked;

each of said first and said second oligonucleotides comprise a plurality of nucleoside subunits with 2'-hydroxyl pentofuranosyl sugar moieties; and

at least one of said first and said second oligonucleotides comprises at least one chemical modification that increases its resistance to single-stranded nucleases or increases its affinity for the other oligonucleotide.

235. (New) The composition of claim 234 wherein at least one chemical modification is a modified internucleoside linkage, a modified sugar moiety or a modified nucleobase.

236. (New) The composition of claim 234 wherein at least one chemical modification is a phosphorothioate linkage.

237. (New) The composition of claim 234 wherein at least one chemical modification is a 2'-substituted sugar modification.

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238. (New) The composition of claim 234 wherein at least one chemical modification is a 2'-alkoxy sugar modification.

239. (New) The composition of claim 234 wherein at least one chemical modification is a 2'-methoxy modification.

240. (New) The composition of claim 234 wherein at least one chemical modification is a 2'-fluoro modification.

241. (New) The composition of claim 234 wherein at least one chemical modification is a 2'-O-methoxyethyl modification.

242. (New) The composition of claim 234 wherein each of said first and said second oligonucleotides independently comprise at least one chemical modification that increases its resistance to single-stranded nucleases or increases its affinity for the other oligonucleotide.

243. (New) The composition of claim 234 wherein said first and said second oligonucleotides comprise at least 17 contiguous nucleotides which are 100% complementary to each other.